REMARKS

Claims 1-4 are pending in the instant application. Claims 1-4 have been rejected. Claim 1, 2 and 4 have been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Election/Restriction Requirement Under 35 U.S.C. §121

The Examiner acknowledges Applicant's election with traverse of the election of species with generic claim 1 and upon reconsideration has withdrawn the species requirement.

II. Objection to Drawings

The drawings as filed July 27, 2001 have been objected to by the draftsman. Applicant filed formal drawings April 9, 2002 and request that these new drawings be considered.

III. Rejection of Claims Under 35 U.S.C. §112

Claims 1-4 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner suggests that Applicant broadly claims a method identifying compounds utilizing a Smad protein or a Smad protein co-repressor, as well as a number of proteins that are art known to act with the family of Smad proteins such as CtPB proteins without providing sufficient structural or functional characteristic of the encompassed proteins.

Applicant respectfully traverses this rejection. Applicant believes that the specification provides a clear description allowing persons of ordinary skill in the art to recognize that Applicant was in possession of the claimed invention at the time of filing. At the time of filing, Smad proteins such as Smad 1-8, Mad, and Medea were known to function both positively and negatively downstream of TGF-β signaling pathways (see page 2, lines 7-11 and page 2, line 25 to page 3, line 7). Further, nucleotide and polypeptide sequences of each species of Smad protein provided in the specification were readily available to the skilled artisan as deposited Genbank sequences in advance of the filing date of the present application (see Table 1).

Table 1

Smad	Submission Date	Accession No.
Smad1	8/2/00	AF295762
Smad2	10/2/97	AF027964
Smad3	9/16/97	AF025300
Smad4	1/10/01	AB053483
Smad5	6/27/97	AF010604
Smad6	11/21/97	AF035528
Smad7	1/12/98	AF042499
Smad8	8/4/99	AF175408
Mad	6/2/94	U10328
Medea	12/18/97	AF039232

Similarly, Smad protein co-repressors such as Evi-1, TGIF, SIP and Schnurri had been shown to interact with Smad proteins in repressing transcription downstream of TGF-β signaling pathways (see page 3, lines 22-30) with nucleotide and polypeptide sequences readily available as deposited Genbank sequences (Table 2).

Table 2

Smad Protein Co-Repressor	Submission Date	Accession No.
Evi-1	4/27/93	M21829
TGIF	7/17/95	X89750
SIP1	2/21/00	AF237679
Schnurri	6/1/95	L42311

Likewise, CtBP proteins were known as general co-repressor proteins prior to the instant invention (see page 8, lines 22-25) with nucleotide and polypeptide sequences of CtBP proteins such as dCtBP, CtBP2 and functional mammalian homologues of dCtBP readily available as deposited Genbank sequences (Table 3).

Table 3

Smad Protein Co-Repressor	**Submission Date**	**Accession No.**
dCtBP	3/5/98	AB011840
CtBP2	4/16/98	AF059735
Human CtBP	10/6/98	U37408
Rat CtBP	7/25/01	NP_062074
Mouse CtBP	10/1/99	AB033122

In addition to the structural and functional information well-known to the skilled artisan, the results provided in instant application disclose that the Smad, Smad protein co-repressor, and CtBP proteins form a complex of interacting proteins that function in TGFβ-pathway induced repression. Accordingly, the applicant has amended claim 1 to recite that the Smad, Smad protein co-repressor, and CtBP proteins function as a complex of interacting proteins that induce repression of transcription. Support for this amendment may be found on page 14, lines 11-21. Withdrawal of this rejection is therefore respectfully requested.

Claims 2 and 4 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner suggests that claim 2 is vague and indefinite in the recitation "co-repressor protein". In response, Applicant has amended claim 2 to recite a Smad co-repressor. Support for this amendment may be found on page 5, lines 10-12.

The Examiner further suggests that claim 4 is vague and indefinite in the recitation "any homologue of CtBP". In response, Applicant has amended claim 4 to recite dCtBP, CtBP2, or a homolog of dCtBP as it is known that homologs of dCtBP, like dCtBP, function as co-repressors and have the ability to bind histone deacetylase (see page 8, lines 22-25) and homologs of dCtBP were well-known in the art at the time of filing (see Table 3, *supra*). Withdrawal of these rejections is therefore respectfully requested.

IV. Rejection of Claims Under 35 U.S.C. §102

Claims 1 and 4 have been rejected under 35 U.S.C. §102(a) as being anticipated by Melhuish and Wotton (December 2000, *J. Biol.*

Chem. 275(50):39762-39766). The Examiner suggests the Melhuish and Wotton disclose an assay wherein the transcriptional repressor activity of Smad2 and CtBP are tested before and after the addition of wild-type and deletion mutants of TGIF, regarded as the test compounds. The Applicant respectfully traverses this rejection.

In an earnest effort to advance the prosecution, Applicant has amended claim 1 to recite that the transcription repressor activity of a Smad protein and a CtBP protein before and after addition of a test compound is determined in the presence of a Smad co-repressor. While Melhuish and Wotton may teach an assay wherein the transcriptional repressor activity of Smad2 and CtBP is determined in the presence of a test compound such as TGIF, this reference does not teach or suggest an assay for identifying compounds that prevent repression of transcription of TGF-β, activin, or BMP signaling wherein the assay comprises determining the level of transcription before and after the addition of a test compound in the presence of a complex of interacting proteins of Smad protein, a Smad protein co-repressor, and a CtBP. Withdrawal of this rejection is therefore respectfully requested.

V. Conclusion

The Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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